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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOSEPH A. SORGE, REINHOLD DIETRICH MUELLER,
GOTHAMI PADMABANDU, NICK ROELOFS, and
HOLLY H. HOGREFE

Appeal 2010-001834
Application 10/734,563
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and
STEPHEN WALSH, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for lack of written description and lack of enablement. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF CASE

The following claim is representative.

1. An Archaeal DNA polymerase comprising at least one amino acid mutation in the exoI motif and an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NOS. 83-108, wherein said Archaeal DNA polymerase is deficient in 3'-5' exonuclease activity.

Cited References
None

Grounds of Rejection

1. Claims 1-10 and 12-21 are rejected under 35 U.S.C. § 112, first paragraph, as being unpatentable for lack of written description.

2. Claims 1-10 and 12-21 are rejected under 35 U.S.C. § 112, first paragraph, as being unpatentable for lack of enablement.

Discussion

1. Claims 1-10 and 12-21 are rejected under 35 U.S.C. § 112, first paragraph, as being unpatentable for lack of written description.

ISSUE

The Examiner concludes that

> The specification does not support the broad scope of the claims which encompass all modifications and fragments of any mutant DNA polymerase comprising the amino acid sequence of SEQ ID NO: 89 and comprising at least one mutation in an exo I,

> II or III motif and another at position V93, that is deficient in 3'-5' exonuclease.

(Ans. 7.)

Appellants contend that the Specification provides a sufficiently detailed description of the claimed genus by structure and a known and disclosed correlation between structure and function and numerous representation members of the genus such that one of ordinary skill in the art would recognize that Appellants were in possession of the claimed invention.

The issue is: Does the Specification evidence a description of the full scope of the elected species of the claims and possession of the claimed invention of the elected species.

PRINCIPLES OF LAW

When the examiner has required the applicant to elect single chemical species for examination, the issue on appeal is the patentability of the single elected species. It is appropriate to limit discussion to that single issue and take no position respecting the patentability of the broader generic claims, including the remaining, non-elected species. *See Ex parte Ohsaka*, 2 USPQ2d 1460, 1461 (BPAI 1987).

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003).

"[T]he written description requirement applies to all claims and requires that the specification objectively demonstrate that the applicant

actually invented—was in possession of—the claimed subject matter." *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d. 1336, 1349 (Fed. Cir. 2010).

> Although many original claims will satisfy the written description requirement, certain claims may not. For example, a generic claim may define the boundaries of a vast genus of chemical compounds, and yet the questions may still remain whether the specification, including original claim language, demonstrates that the applicant has invention species sufficient to support a claim to the genus.

Id. at 1350.

A sufficient description of a genus requires the disclosure of either a representative number of species falling within the scope of the genus, or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus. *Id.* In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997).

FINDINGS OF FACT

The Examiner's fact finding can be found in the Answer at pages 4-9. Additional findings of fact follow.

1. The Specification at page 6 describes that mutations in exo I motif are selected from aspartic acid to threonine, aspartic acid to alanine and glutamic acid to alanine.

2. Figure 7B shows the exo I motif is represented by the consensus amino acid sequence DXE. The exo II motif is represented by the consensus amino acid sequence $NX_{2-3}(F/Y)D$. The exo III motif is represented by the consensus amino acid sequence YX_3D.

3. The Specification figure 6A discloses V93 mutants of Pfu DNA polymerase.

4. SEQ ID NOs: 25 and 26 are deletion mutants of V93.

5. The Specification discloses in Fig.7 B. the locations of exoI, II and III.

6. SEQ ID NO:89 is the wild-type Pfu DNA polymerase.

ANALYSIS

Appellants elected wild-type Pfu DNA polymerase of SEQ ID NO: 89 in response to the election of species requirement. (App. Br. 14.) Figure 7B similarly shows the amino acid sequence of Pfu DNA polymerase including the locations of the V93 and exoI, II and III mutations. We limit our discussion to the elected species, wild-type Pfu DNA polymerase of SEQ ID NO: 89 with at least one amino acid mutation in the exoI motif and an amino acid mutation at V93, and take no position respecting the patentability of the broader generic claims, including the remaining, non-elected species. *See Ex parte Ohsaka*, 2 USPQ2d at 1461.

The Examiner concludes that the Specification only provides that Archaeal DNA polymerases and compositions and kits comprising said Archaeal DNA polymerases, wherein the Archaeal DNA polymerase comprises the amino acid sequence of the Pfu DNA polymerase, SEQ ID NO: 89, with an amino acid mutation in an exoI, exo II or exo III motif or a combination thereof and an amino acid mutation at position V93 in the

amino acid sequence of SEQ ID NO: 89, wherein the Archaeal DNA polymerase is deficient in 3'-5' exonuclease activity, encompassed by these claims. (Ans. 4.) Thus the Examiner appears to agree that the claimed mutations of V93 and exoI of SEQ ID NO: 89 are disclosed and described in the Specification. See particularly, Spec. 7-17 and Figures.

The Examiner argues

> there is no disclosure of any particular structure to function/activity relationship in the disclosed species that would put one in possession of the genus of all possible mutant Archaeal DNA polymerases comprising an amino acid mutation in an exoI, exo II or exo III motif or a combination there of and an amino acid mutation at position V93 in an amino acid sequence of SEQ ID NO:89, that are deficient in 3'-5' exonuclease activity.

(Ans. 4-5.)

Appellants contend that

> It was known in the art that the 3' to 5' exonuclease domain in DNA polymerases comprises three conserved motifs (exo I, exo II and exo III). [] The exo I motif is represented by the consensus amino acid sequence DXE. [] The exo II motif is represented by the consensus amino acid sequence $NX_{2-3}(F/Y)D$. [] The exo III motif is represented by the consensus amino acid sequence YX_3D.
>
> It was also known in the art that DNA polymerases with 3' to 5' exonuclease activity, like Archaeal DNA polymerases, could be mutated in the conserved exo I, exo II, or exo III motifs to generate mutant DNA polymerases having reduced or abolished 3' to 5' exonuclease activity. Thus, there was a known correlation in the art between the conserved exo I, exo II, and exo III motifs of DNA polymerases and 3' to 5' exonuclease activity. This known correlation between structure and function is not disputed by the Examiner.

(App. Br. 15-16.)

We are persuaded by Appellants that there is a structure to function relationship between exo I, II and III mutations and exonuclease activity. With respect to the elected species the Specification describes SEQ ID NO: 8, Figure 7B similarly shows the amino acid sequence of Pfu DNA polymerase including the locations of the V93 and exoI, II and III mutations. Thus again we conclude that the Specification describes the elected species and representative species including at least one amino acid mutation in the exoI motif and an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NOS. 89, wherein said Archaeal DNA polymerase is deficient in 3'-5' exonuclease activity.

We conclude that Appellants have reasonably described representative species of the elected invention and that Appellants were in possession of the elected invention claim scope.

2. Claims 1-10 and 12-21 are rejected under 35 U.S.C. § 112, first paragraph, because the Specification, while being enabling for a Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO: 89 with an amino acid substitution at position V93, does not reasonably provide enablement for any possible Archaeal DNA polymerase comprising at least one amino acid mutation in an exo I, exo II or exo III motif and another amino acid mutation at position V93 in an amino acid sequence selected from SEQ ID NO:89, wherein said polymerase is deficient in 3'-5' exonuclease activity.

ISSUE

The issue is: Does the specification enable the elected species of claim 1?

PRINCIPLES OF LAW

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

FINDINGS OF FACT

6. According to the Examiner, the "specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." (Ans. 5.)

7. The Examiner finds that

> Claims 1-10 and 12-21 are so broad as to encompass any possible polymerase that originated as an Archaeal DNA polymerase and further comprises at least one amino acid mutation in an exoI, exo II or exo III motif and another amino acid mutation at position V93 in an amino acid sequence selected from SEQ ID NO:89, wherein said polymerase is deficient in 3'-5' exonuclease activity.

(*Id.* at 6.)

8. The Examiner finds that

> The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant DNA polymerases broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place minor if any structural limits on the claimed mutant DNA polymerases.

(Ans. 6.)

9. The Examiner finds that

> The claimed genus of DNA polymerase is interpreted as not being structurally limited beyond the necessary mutation positions and this includes the vast types of mutations that may occur at these mutation positions. These referred to mutations include but are not limited to one or more amino acid substitutions, one or more amino acid insertions, a truncation or an internal deletion (see specification page 11, lines 2-4) or any additional type of post-translational modification at these referred to amino acid positions. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

(*Id.* at 6-7.)

10. The Examiner finds that,

> in this case, the disclosure is limited to those instantly disclosed mutant Pfu DNA polymerases that are deficient in 3'-5' exonuclease activity and comprise the amino acid sequence of SEQ ID NO: 89 with an amino acid substitution mutation at position V93 of SEQ ID NO:89.

> While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

(Ans. 7.)

11. The Examiner concludes that "[t]he specification does not support the broad scope of the claims which encompass all modifications and fragments of any mutant DNA polymerase comprising the amino acid sequence of SEQ ID NO: 89 and comprising at least one mutation in an exo I, II or III motif and another at position V93, that is deficient in 3'-5' exonuclease activity." (*Id.*)

ANALYSIS

The Examiner concludes that the claims are enabled for a Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO:89 with an amino acid substitution at V93, but does not reasonably provide enablement for any possible Archaeal DNA polymerase comprising at least one amino acid mutation in an exoI, exo II or exo III motif and another amino acid mutation at position V93. (Ans. 5.) The Specification figure 6A discloses V93 mutants of Pfu DNA polymerase. SEQ ID NO: 25 and 26 are deletion mutant as V93. The Specification discloses in Fig.7 B. the locations of exoI, II and III. Thus, limiting our review to the elected species, we conclude that the Specification enables the production of an Archaeal DNA

polymerase comprising at least one amino acid mutation in the exoI motif and an amino acid mutation at V93 in an amino acid sequence selected from one of SEQ ID NO. 89 wherein said Archaeal DNA polymerase is deficient in 3'-5' exonuclease activity consistent with the elected species of Pfu SEQ ID NO:89.

We do not find that the Examiner has provided sufficient evidence of lack of enablement on the evidence before us. The Specification provides several examples of mutations of V93 of Pfu polymerase including various deletion mutants. We conclude that the Specification therefore enables such mutations of V93 of Pfu polymerase. We also find that Figure 7B discloses the location of possible mutations of exo I, II and III of Pfu polymerase. The Specification discloses that these mutations result in reduced or abolished 3' to 5' exonuclease activity. One of ordinary skill in the art would be able to prepare mutants of exo I , II and III based on the disclosure. We conclude that this disclure enables an Archaeal DNA polymerase of the elected species.

CONCLUSION OF LAW

The evidence of record does not support the Examiner's rejection of lack of enablement and lack of written description rejections with respect to the elected species.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

REVERSED

cdc

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